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FAMILIAL APPEARANCE OF PRIMARY OPEN ANGLE GLAUCOMA

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SUMMARY – The aim of the study was to point out the role of inheritage of primary open angle glaucoma (POAG) and frequency of POAG among other glaucoma diseases.

The study included 52 relatives from 12 families with family history of POAG through 3 generations. The examination consisted of complete ophthalmologic status, automated perimetry and optic nerve photography. A detailed anamnesis and family trees were taken. Individuals were diagnosed with POAG if they fulfilled two or three of the criteria for making a diagnosis: the level of intraocular pressure visual field loss or characteristic disc appearance. Subjects were considered "suspected POAG" if they fulfilled only one of the preceding three criteria. All three parameters had to be normal for an individual to be considered unaffected. Seven relatives (l2%) were diagnosed with P0AG, fifteen (29%) relatives were classified as glaucoma suspects. Siblings of POAG patients had the highest risk of POAG developing compared with children or other blood relatives.

The study presented results of investigation the frequency of POAG among other glaucoma diseases and 16% patients had a family history of POAG at least in 3 generations. Detailed anamnesis confirms familial appearance of POAG and examination of all available members enables the discovery of new cases (12%).

Introduction

Primary open angle glaucoma (POAG) has been identified as a chronic progressive opticoneuropathy with symptoms: intraocular pressure (IOP) greater than 21 mmHg without treatment (diurnal tension curve), characteristic glaucomatous damage on the optic nerve head (cup/disc ratio), glaucomatous defects corresponding to the optic disc damage may be present on visual field, and open anterior chamber angle established by gonioscopy.[1] The level of IOP, cup/ disc ratio and characteristic visual field loss are at the same time the criteria for making diagnosis.

Hereditary predisposition to glaucoma was investigated and suggested by many authors. With the developments in molecular biology and genetics, the understanding of the genetic basis of the glaucomas has advanced rapidly and 8 chromasomal loci have been reported: 2 for congenital glaucomas and 6 for POAG.[2] Mutations in the trabecular meshwork induced glucocorticoid response (myocilin/TIGR) gene were determined to cause most cases of autosomal dominant juvenile g1aucoma and to play a role in adult POAG.[3] The increased risk of glaucoma in family members of patients with POAG has been recognized for a long time, and several studies have screened relatives of patients with POAG for manifestation of the disease.[4,5]

Cross-sectional epidemiological studies have shown that 10-50% of POAG patients report a family history of glaucoma. Furthermore, a declared family history of glaucoma is a risk factor for progression of ocular hypertension into POAG.[6,7,8]

Epidemiologic data from the Baltimore Eye Survey, the largest population - based study of patients with POAG and unaffected controls, confirm that a fami1y history of POAG is an important risk factor in the development of the disease.[6] The Barbados Eye Study also suggested that older men with a family history of glaucoma are most likely to have glaucoma.[9]

We present the results of our investigations of 52 re1atives of patients with POAG from l2 families where

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POAG appears at least through 3 generations. We systematically evaluated these patients and assigned them to disease categories, using a currently accepted definition of POAG and standardized screening methods.

Participants and Methods

Families enrolled in this study were recruited from the Cabinet for Glaucoma, University Department of Ophthalmology, Sestre milosrdnice University Hospital in Zagreb, Croatia. Consent was obtained from patients to contact other family members and to participate in the study. All available family members were invited to undergo an ocular examination, visual filed testing and optic nerve head photography. With a detailed family anamnesis and evaluated family trees, clinical examination included refraction, applanation tonometry and ophthalmoscopy. Visual field testing was done by the use of standard full-threshold automated static perimetry (dG2 program on the Octopus Visual Field Analyzer). Slit-lamp examination and gonioscopy were performed. Families with probands with closed or narrowed angles and those with pigmentary glaucoma or pseudoexfoliation were excluded from the study. No families with juvenile glaucoma participated in this study. IOP measurements were taken twice and averaged. Stereoscopic photographs of the optic nerve head were taken. The individuals were diagnosed with POAG if they fulfilled two or three of the following criteria: 1) an IOP greater than or equal to 22 mmHg in either eye; 2) visual field defects in either eye that were compatible with those which are characteristic of glaucoma as defined in the study of Katz et al;[10] 3) optic nerve head configuration compatible with glaucoma in either eye as determined by two indepedent examiners. Subjects were considered "suspected POAG" if they fulfilled only one of the preceding three criteria. All three parameters had to be normal for an individual to be considered unaffected at the time of the study.

Table 1. The results according to the criteria that determine diagnosis

Diagnosis	Participants	%
Normal	30	59%
Suspect	15	29%
Glaucoma status	7	12%
Total	52	100%

Results

Cabinet for Glaucoma, University Department of Ophthalmology, has treated 4186 patients, among which 670 (16 %) had a family history of POAG at least through 3 generations.

A total of 52 individuals from l2 families were examined; there were 23 affected men and 29 affected women, with a male/female ratio of 0,70. The individuals ranged in age from 24 to 77.

According to the criteria with determined diagnosis of POAG, 30(59%) relatives were normal, 15(29%)relatives were suspect and 7(12%)out of the total number were unregistered cases until then (Table 1). Excluding spouses, 52 relatives were distributed as follows: 16 parents, l2 siblings, 18 children and 6 other blood relatives. Seven relatives (12%), 5 siblings, 1 parent and 1 other blood relative were found to have POAG. Fifteen relatives (29%)- 5 parents, 5 siblings, and 5 other blood relatives- were identified as glaucoma suspects by our investigations. All the children were normal (Table 2). Three out of 7 relatives who were diagnosed with glaucoma had an elevated IOP, abnormal visual fields and optic disc changes consistent with glaucoma; one of them had an elevated IOP and abnormal visual field; two of them had an elevated IOP and optic disc changes; and one of them had an abnormal visual field and optic nerve head configuration compatible with glaucoma.

Table 2. Distribution of 52 relatives, relationship to proband, diagnosis and glaucoma disease

Relation to proband	normal	Suspect	Glaucoma disease	Total
Parent	10	5	1	16
Sibling	2	5	5	12
Chlid	18	–	–	18
Other blood relatives	–	5	1	6
Total number of relatives	30	15	7	52

Table3. Abnormal parameters (+) leading to diagnosis

Elevated intraocular pressure	Abnormal visual field	Abnormal optic disc	Number of patients	Disease
+	+	+	3	glaucoma
+	+	–	1	glaucoma
+	–	+	2	glaucoma
–	+	+	1	glaucoma
+	–	–	4	suspect
–	+	–	7	suspect
–	–	+	4	suspect

Out of the 15 patients identified as POAG suspects, 4 of them had optic disc changes consistent with glaucoma, 4 of them had an elevated IOP and 7 of them had an abnormal visual field (Table 3).

Discussion

Cross-sectional epidemiological studies have shown that 10 to 50% of POAG patients report a family history of glaucoma.[6,7,8] We have found 16 % of the patients with family history of glaucoma recruited from Cabinet for Glaucoma, University Department of Ophthalmology.

It is well established that POAG is more likely to affect individuals with a family history of the disease.[8,9,11] There is a definite increased prevalence of POAG among first - degree relatives of the patients with the disease with as many as 2,8 to 13,5% being affected, compared with a prevalence of 0,5 % to 2,0 % in the general population .[2,12,13] Seven out of 52 family members (12%) fulfilled the diagnostic criteria for POAG. This result is in accordance with some other studies: Randall at al 30%,[14] Mc Naught et al 7%.[15] We also found a grater risk for siblings than for children or other blood relatives to develop glaucoma.

This study has also shown that children in family have never showed glaucoma symptoms. It is possible, however, that this is an age related issue and that children and siblings are at an equivalent risk for the disease, but may not manifest POAG until they are older. Longitudinal studies are necessary to clarify this issue.

Our data demonstrate that in families with POAG in at least 3 generations a large proportion of first-degree and other blood relatives either have glaucoma or have an abnormality in one of the three parameters that are associated with the disease. In such families, we have been recommending complete ophthalmologic examinations in all adult relatives. Studies of larger numbers of families are necessary to verify our findings.

Conclusion

A detailed anamnesis confirms familial appearance of POAG and examination of all available members enables the discovery of new cases (12%).

In the absence of biochemical and genetic markers for the disease in most cases, we continue to rely on clinical examinations for the early detection of glaucoma in family members.

References

1. STONE EM, FINGERT JH, ALWARD JH et al. Identification of a gene that causes primary open angle glaucoma. Science 1997;275(5300):668-670.
2. PERKINS ES. Family studies in glaucoma. Br J Ophthalmol. 1997; 58:529-535.
3. WIGGS JL, ALLINGHAM RR, VOLRATH D, et al. Prevalence of mutations in TIGR/Myocilin in patients with adult and juvenile primary open angle glaucoma. Am J Hum Genet 1998;63:1549-52.
4. SARAFAZI M. Recent advances in molecular genetics of glaucomas. Hum Mol Genet 1997;6:1667-77.
5. QUIGLEY HA. The search for glaucoma genes-implications for pathogenesis and disease detection (editorial). N Engl J Med 1998; 338:1063-4.
6. TIELSCH JM, KATZ J, SOMMER A, et al. Family history and the risk of primary open angle glaucoma. The Baltimore Eye Survey. Arch Ophthalmol 1994;112:69-73.
7. ROSENTHAL AR,PERKINS ES. Fami1y studies in glaucoma, Br J Ophthalmol 1985;69:664-7,
8. LESKE MC. Warheit-Roberts L, Wu SY. Open angle glaucoma and ocular hypertension: the Long Island Case-control Study. Ophthalmic Epidemiol. 1996;3:86-96.

9. NEMESURE B, LESKE MC, HE Q, MENDELL N. Analysis of reported family history of glaucoma: a preliminary investigation. The Barbados Eye Study Group. Ophthalmic Epidemiol 1996;3:135-41.
10. KATZ J, TIELSCH JM, QUIGLEY HA, SOMMER A. Automated perimetry detects visual field loss before manual Goldmann perimetry. Ophthalmology 1995;102:21-6.
11. LEIGHTON DA. Survey of the first degree relatives of glaucoma patients. Trans Ophthalmo1 Soc UK 1976;96:28-32.
l2. BECKER B, KOLKER AE, ROTH FD. Glaucoma family study Am J Ophthalmol 1960;50:557-67.
13. MILLER SJH, PATERSON GD. Studies on glaucoma relatives. Br J Ophthalmol 1962;46:513 -22.
14. RANDALL L, SHARATH C, ELIAS I. Screening relatives of patients with familial chronic open angle glaucoma. Ophthalmology 2000; 107:1294-97.
15. McNAUGHT AI, ALLEN JG, HEALEY DL, MCCARTNEY PJ, COOTE M, WONG TL, CRAIG J et al. Accuracy and implications of a reported family history of glaucoma. Arch Ophthalmol 2000;118:900-04.

Sažetak

OBITELJSKO POJAVLJIVANJE PRIMARNOG GLAUKOMA OTVORENOG KUTA

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Cilj istraživanja bio je naglasiti ulogu nasljeđa kod primarnog glaukoma otvorenog kuta te ukazati na njegovu učestalost među drugim glaukomskim oboljenjima. Ukupno je 52 člana iz 12 obitelji kod kojih se primarni glaukom otvorenog kuta pojavljuje kroz najmanje 3 generacije, obuhvaćeno je ispitivanjem. Pored detaljne obiteljske anamneze i izrade obiteljskog stabla, kliničko ispitivanje obuhvaćalo je: sveukupni oftalmološki pregled, automatiziranu perimetriju i fotografiju glave vidnog živca. Ispitanici su utvrđeni kao glakomski bolesnici ako su ispunjavali 2 ili 3 uvjeta koji čine dijagnozu: visina intraokularnog tlaka, ispadi u vidnom polju te karakterističan izgled glave vidnog živca. Granični slučajevi ispunjavali su samo jedan postavljeni uvjet, a zdravi ispitanici su imali sve parametre u granici normale. Sedam rođaka (12%) dijagnosticirano je kao primarni glaukom otvorenog kuta a 15 (29%) kao granični slučajevi. Braća i sestre pacijenata s primarnim glaukomom otvorenog kuta imaju veći rizik pojave oboljenja u usporedbi s djecom ili ostalim rođacima.

Studija pokazuje da je među glaukomskim pacijentima 16% onih s pozitivnom obiteljskom anamnezom za primarni glaukom otvorenog kuta kroz najmanje 3 generacije. Detaljna obiteljska anamneza potvrđuje obiteljsku pojavu primarnog glaukoma otvorenog kuta, a ispitivanje svih dostupnih članova omogućuje otkrivanje novih, dotad neregistriranih slučajeva - l2%.

Key words: *glaucoma*, *heredity*